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Re-evaluation Note REV2016-16

Special Review of Acephate: Proposed Decision for Consultation

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1.0 Introduction

Pursuant to subsection 17(2) of the *Pest Control Products Act*, the Pest Management Regulatory Agency (PMRA) has initiated a special review of pest control products containing acephate based on the European Commission decision (2003) to prohibit the use in Europe due to human health and environmental concerns. The initiation of the special review was announced in December 2013 (Canada, 2013).

As required by subsection 18(4) of the *Pest Control Products Act*, the PMRA has evaluated the aspects of concern related to the pest control products containing acephate that prompted the special review. The aspects of concern are relevant to the human health and environment.

2.0 Uses of Acephate in Canada

Acephate is an organophosphate insecticide used to control a broad range of insect pests on a wide variety of sites including forests and woodlots, right of ways and municipal parks, greenhouse ornamentals, terrestrial food and feed crops and outdoor ornamentals. Acephate is applied using conventional ground application equipment, soil injection, tree trunk injection and implant cartridges by farmers, farm workers and professional applicators. All currently registered pest control products containing acephate (Appendix I) are considered in this special review.

3.0 Aspects of Concern that Prompted the Special Review

Based on the review of the European decision (European Commission, 2003), the PMRA has identified the aspects of concern that prompted the special review of pest control products containing acephate as:

- Acute dietary exposure;
- Potential risks to non-target terrestrial invertebrates, birds and mammals; and
- Potential risks to aquatic species.

4.0 PMRA Evaluation of the Aspects of Concern that Prompted the Special Review

Following the initiation of the special review of acephate, the PMRA requested information from provinces and other relevant federal departments and agencies, in accordance with subsection 18(2) of the *Pest Control Products Act*. No additional information was received.

In order to evaluate the aspects of concern for acephate, the PMRA has considered currently available relevant scientific information, which includes the European decision, information considered for the re-evaluation of acephate including any comments received in response to the acephate proposed re-evaluation decision (Canada, 2016).

No information related to the aspects of concern was identified in the Canadian incident report database

4.1 Acute Dietary Exposure

Methamidophos is a major metabolite of acephate and may be formed in food and drinking water as a result of acephate use; thus separate acute dietary exposure and risk assessments were conducted for both acephate and methamidophos. All previous uses of methamidophos as an active ingredient have been excluded in the assessment, as these uses are being phased out in Canada and the United States.

For assessing risks from potential residues in drinking water, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

The acephate database contains the full complement of required studies including developmental toxicity studies in mice, rats and rabbits and a three generation reproductive toxicity study in rats. A set of comparative cholinesterase toxicity studies and a developmental neurotoxicity study in rats were also available for acephate. With respect to potential prenatal and postnatal toxicity, decreased pup survival (considered a serious endpoint) was observed in the 3-generation reproductive toxicity study in rats. However, concern for this endpoint was tempered by the presence of maternal toxicity (effects on body weight) at the same dose level. In a developmental toxicity study in mice, there was an increased incidence of external and skeletal abnormalities in the presence of maternal toxicity. In the rat and rabbit developmental toxicity studies, no evidence of teratogenicity or sensitivity of the young was noted. In the comparative cholinesterase studies conducted with rats, effect levels were established based on the inhibition of brain cholinesterase activity. Overall, the comparative cholinesterase studies revealed no sensitivity of the young. Therefore, the database for acephate is considered complete for determining toxicity to the young. Since there is low concern for sensitivity of the young and adequate margins exist for serious endpoints noted in the database, the *Pest Control Products Act* factor for acephate was reduced to 1-fold (Canada, 2016).

The methamidophos database also contains the full complement of required studies including developmental toxicity studies in rats and rabbits and a two generation reproductive toxicity study in rats. With respect to potential prenatal and postnatal toxicity, there was no evidence of teratogenic effects and no additional sensitivity of the fetus following in utero exposure to methamidophos in rats and rabbits. In the reproduction study, no sensitivity of the young was demonstrated at the levels tested. An additional 3-fold safety factor has been used to provide an additional safeguard for the delayed neurotoxic potential of methamidophos. On the basis of the low concern for prenatal and postnatal toxicity, and considering the additional safety factor to account for database concerns (i.e. delayed neurotoxic potential), the *Pest Control Products Act* factor for methamidophos was reduced to 1-fold (Canada 2007).

For acute dietary exposure to acephate, an acute reference dose (ARfD) of 0.0017 mg/kg bw for all populations was selected based on a LOAEL of 0.5 mg/kg bw/day from an acute cholinesterase study in rat (Canada, 2016). An additional uncertainty factor of 3-fold was applied for the lack of a NOAEL (composite assessment factor is 300).

This endpoint is the most sensitive endpoint available in the database, for a single exposure and is protective of other neurological and systemic effects. The ARfD is considered protective of all populations including infants and children.

For acute dietary exposure to methamidophose, an acute reference dose (ARfD) of 0.0003 mg/kg bw for all populations was selected based on a NOAEL of 0.1 mg/kg bw/day from a developmental neurotoxicity study in rat (composite assessment factor is 300) (Canada, 2016). The ARfD is considered protective of all populations including infants and children.

Acute dietary exposure is not of concern ranging from 23-49% of the ARfD for acephate, and 33-56% of the ARfD for methamidophos, with the cancellation of potato use, reduced application rates, reduced number of applications per season, and increased application intervals (See Appendix II for proposed label amendments).

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, as well as from all known or plausible exposure routes (oral, dermal, inhalation). In the case of acephate, there is potential exposure from acephate foliar application to trees and ornamentals in residential areas, which could co-occur with dietary exposure from food and drinking water. To mitigate this risk, the PMRA proposes that commercial application of acephate products in residential areas not be permitted (See Appendix II for proposed label amendments). With the proposed mitigation, acute aggregate exposure is limited to food and drinking water which is not of concern for acephate and methamidophos (as described above).

The PMRA will quantitatively assess the cumulative risks of organophosphate pesticides once all individual organophosphates have been re-evaluated. This cumulative assessment will consider potential exposure to all organophosphate pesticides causing toxicity in the same manner.

4.2 Potential risks to non-target terrestrial invertebrates, birds and mammals

The risk assessment of acephate and its transformation product methamidophos to terrestrial organisms was based upon an evaluation of toxicity data for earthworm, bees, small mammals and birds. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with acephate.

Invertebrates

Based on a tier one risk assessment (with laboratory data), acephate was shown to be toxic to bees when exposed to high enough concentrations, and therefore a potential risk to adult foraging bees from contact exposure (Canada, 2016). Foliage residue toxicity studies indicate that acephate/methamidophos exhibit toxic effects to honeybees and beneficial insects from 2 to 24 hours after application, indicating residual toxicity. Based on higher tier studies, there is also a potential for brood and adult toxicity from dietary exposure to residues in pollen and/or nectar brought back to the hive from application before bloom and during bloom. As such, mitigation measures are required for the special review (See Appendix II for proposed label amendments). With the proposed mitigation measures, exposure to terrestrial invertebrates is not of concern.

Birds and Mammals

Because exposure is dependent on the body weight of the organisms and the amount and type of food consumed, the risk assessment for birds and mammals considers a set of generic body weights (20, 100, 1000 g for birds and 15, 35, 1000 g for mammals) and food preferences (small insects for insectivores, fruits for frugivores, grain and seeds for granivores and leaves and leafy crop for herbivores.

Acephate transforms quickly to methamidophos in the environment (dissipation time to 50% of less than 2 days). Methamidophos is classified as very highly toxic to birds for oral acute, subacute dietary, dermal and inhalation exposures based on laboratory data. Methamidophos is classified as highly toxic to mammals on an acute basis.

Many field studies show that adverse effects from acephate do not occur at the time of application; rather, they occur at one to two days after application. As a result, researchers interpreted that toxicity was due to the transformation product, methamidophos. Field studies have indicated that there is a high acute risk to birds. Data from field studies suggested that when acephate alone was applied, both acephate and methamidophos were found in animals and in their food items. Birds have been shown to have marked brain cholinesterase (ChE) inhibition for at least up to 33 days after acephate application at a rate as low as 560 g a.i./ha.

As acephate transforms quickly to methamidophos, which is more toxic than acephate, the risk assessment is based on a consideration that acephate application is an equivalent of 50% of methamidophos. Therefore, application rates were recalculated from acephate to methamidophos based on molecular ratio of 0.77 and methamidophos toxicity endpoints were used to determine the risk to birds and mammals. Assessment of risk of acephate plus methamidophos indicated a potential risk to birds and mammals feeding on the treated field, but very few exceedances of the level of concern when feeding adjacent to the treated field (Canada, 2016). The assessment is considered to be conservative and assumed 100% of the food consumed is contaminated. The potential risk is expected to be lower as birds and mammals would not typically forage on a single food source. All current acephate labels include wording indicating toxicity to birds and mammals. No further mitigation is required.

4.3 Potential risks to aquatic organisms

Acephate is practically non-toxic to moderately toxic to freshwater and marine species. Methamidophos is very highly toxic to aquatic invertebrates and slightly to moderately toxic to other aquatic species. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with acephate.

The risk assessment indicates that there is a potential chronic risk to aquatic invertebrates from acephate alone, but it is not a concern (RQ 1.1). However, methamidophos, the major transformation product of acephate is more toxic. It is very highly toxic to aquatic invertebrates (LC_{50} < 0.1 mg a.i./L), slightly toxic to freshwater fish on an acute basis (LD_{50} = 10–100 mg a.i./kg), and moderately toxic to estuarine/marine organisms (LC_{50} = 1-10 mg a.i./kg).

As acephate transforms quickly to methamidophos, and being more toxic than acephate, (similar to the terrestrial scenario) the risk assessment has been based on the assumption that acephate application is an equivalent of 50% of methamidophos and methamidophos toxicity endpoints were used to determine the potential risk. The risk assessment shows that there is acute risk to freshwater invertebrates and negligible risk to fish, amphibians and marine invertebrates (Canada, 2016). Buffer zones are required as part of the special review (See Appendix II for proposed label amendments). With the proposed mitigation measures, exposure the aquatic species is not of concern.

5.0 Proposed Special Review Decision for Acephate

Evaluation of available scientific information related to the aspects of concern indicated that the registered products containing acephate do not pose unacceptable risk to human health and the environment with the proposed mitigation measures. On this basis, the PMRA is proposing to confirm the current registration of products containing acephate for sale and use in Canada pursuant to subsection 21(1) of the *Pest Control Product Act*, with the proposed label amendments outlined in Appendix II.

This proposed special review decision is a consultation document.[1] The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

6.0 Next Steps

Before making a special review decision on acephate, the PMRA will consider all comments received from the public in response to this consultation document. A science-based approach will be applied in making a final decision on acephate. The PMRA will then publish a special review decision document, which will include the decision, the reasons for it, a summary of the comments received on the proposed decision and the PMRA's response to these comments.

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Appendix I Registered Products Containing Acephate as of 25 August 2016

Registration Number	Marketing Class	Product Name	Formulation	Guarantee
14225[1]	Commercial	ORTHENE 75% SOLUBLE POWDER SYSTEMIC INSECTICIDE	SOLUBLE POWDER	75%
21568	Commercial	ACECAP 97 SYSTEMIC INSECTICIDE IMPLANTS	SOLUBLE POWDER	0.773 g/cartridge implant
22109	Technical	ORTHENE TECHNICAL	SOLUBLE POWDER	99.78%
27917	Technical	ACEPHATE TECHNICAL	SOLUBLE POWDER	98%
29499	Commercial	ORTHENE 97% PELLET	PELLETS	97%

[1] Proposed for cancellation PRVD2016-01

Appendix II Label Amendments for Products Containing Acephate

A. The following label statements are proposed for end-use products formulated as pellet and cartridge implants:

PRECAUTION STATEMENTS

The following label statements are proposed when product is applied as spray:

> This product cannot be applied as a foliar application in residential areas. Residential areas are defined as any use site where bystanders including children could be exposed during or after application. This includes homes, schools, public buildings or any other areas where the general public including children could be exposed.
>
> Apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

ENVIRONMENTAL PRECAUTIONS:

The following label statements are proposed for PELLET formulation:

> **TOXIC** to bees. Bees may be exposed through direct spray, spray drift, and residues on/in leaves, pollen and nectar in flowering crops and weeds. Minimize spray drift to reduce harmful effects on bees in habitats close to the application site. Avoid applications when bees are foraging in the treatment area in ground cover containing blooming weeds. To further minimize exposure to pollinators, refer to the complete guidance "Protecting Pollinators during Pesticide Spraying – Best Management Practices" on the Health Canada website (www.healthcanada.gc.ca/pollinators). Follow crop specific directions for application timing.
>
> Avoid application during the crop blooming period. If applications must be made during the crop blooming period, restrict applications to evening when most bees are not foraging. When using managed bees for pollination services, DO NOT apply during the crop blooming period or during the 9 day period before the crop blooms.
>
> **TOXIC** to birds, mammals and aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE.

Add to DIRECTIONS FOR USE:

The following label statements are proposed for PELLET formulation:

To protect pollinators, follow the instructions regarding bees in the Environmental Precautions section. TOXIC to bees. Avoid application during the crop blooming period. If applications must be made during the crop blooming period, restrict applications to evening when most bees are not foraging. When using managed bees for pollination services, DO NOT apply during the crop blooming period or during the nine day period before the crop blooms.

To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.

Avoid application when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

Add to DIRECTIONS FOR USE:

Field sprayer application: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) fine classification. Boom height must be 60 cm or less above the crop or ground.

DO NOT apply by air.

Buffer zones:

Uses of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands).

Method of application	Crop	Buffer Zones (meters) Required for the Protection of:	
		Freshwater Habitat of Depths:	
		Less than 1 meter	Greater than 1 meter
Field sprayer	tobacco	2	1

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

B. The following label statements are proposed for uses associated with the product formulated as a soluble powder (Registration No. 14225).

DIRECTIONS FOR USE

Number of Applications:
Consult table below for the number of applications and application intervals per crop.

Crop	Maximum Rate (kg a.i./ha	Maximum Number of applications per Year	Minimum Application Interval (days)
Bell Peppers	0.56	2	14
Brussels Sprouts	0.56	2	14
Cabbage	0.56	2	14
Cauliflower	0.56	2	14
Head Lettuce	0.56	2	14
Celery	0.56	2	14
Sweet Corn	0.56	2	14
Seed Corn	0.56	2	14

ENVIRONMENTAL PRECAUTIONS:

For applications on crops that are highly attractive to pollinators (cranberry and outdoor ornamentals excluding coniferous evergreens), or when using managed bees for pollination services:

DO NOT apply during the crop blooming period or during the 9-day period before the crop blooms.

Add to DIRECTIONS FOR USE:

For cranberry and outdoor ornamentals excluding coniferous evergreens, include:

TOXIC to bees. **DO NOT** apply during the crop blooming period or during the 9-day period before the crop blooms.

Add to DIRECTIONS FOR USE:

Airblast application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

Method of application	Crop		Buffer Zones (metres) Required for the Protection of: Freshwater Habitat of Depths: Less than 1 m	Greater than 1 m
Field sprayer	Cabbage, cauliflower, Brussels sprouts, head lettuce, celery, corn (seed and sweet), tomato, sweet pepper, cranberry, ornamentals, shade trees, Christmas tree plantations, farm woodlots, tree nurseries, shelter belts, rights-of-way, municipal parks		2	1
Airblast	Ornamentals, shade trees, flowers (field grown), Christmas tree plantations, farm woodlots, tree nurseries, shelter belts, rights-of-way, municipal parks	Early growth stage	5	2
		Late growth stage	3	2

Reference List

Published Information:

PMRA no.	Reference
2680115	European Commission, 2003. Commission Decision of 25 March 2003 concerning the non-inclusion of acephate in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing this active substance. DACO 12.5
2680124	European Commission, 2002. Review report for the active substance acephate. 31 May 2002. DACO 12.5
2601494	Canada, 2016. Pest Management Regulatory Agency. Proposed Re-evaluation Decision Acephate. PRVD2016-01.
2405939	Canada, 2013. Pest Management Regulatory Agency. Re-evaluation Note REV2013-06, *Special Review Initiation of 23 Active Ingredients.*